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THE THEORETICAL EFFECTIVENESS OF ADVERSE SELECTION

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As is well known, inherited recessive defects are difficult to eradicate from a large population. Even with selection so rigorous that no individual homozygous for a particular recessive ever leaves offspring, the character will be carried by heterozygous individuals for many generations. Among other theoretical and practical problems involved, the difficulty of eliminating recessive inherited defects raises the question of the value of sterilization and segregation for improving the heredity of the human species.

It is practically impossible ever completely to eliminate a recessive character from a large, freely interbreeding population; nevertheless, by adverse selection the proportion of affected individuals in a population can be reduced. The important question is how much reduction in the proportion of defective individuals in a population can be obtained.

The theoretical effectiveness of adverse selection against a character produced by a single recessive factor may easily be calculated. For a simple hypothetical beginning, let us assume that in a certain population the number of recessive defective genes, *a,* equals the number of normal genes, *A.* Let us further assume completely random mating and equal fertility for all genetic combinations. In such a population the proportional number of individuals in each generation for each of the three Mendelian classes will become $1AA + 2Aa + 1aa$, and these proportions will be continued in all subsequent generations indefinitely, unless selection or mutation takes place. The defective recessive character will be evident, of course, only in the homozygous condition *aa,* which theoretically occurs in one-fourth of the population.

Let us now allow all the homozygous dominant (normal) individuals and heterozygous (normal appearing) individuals of such a population to mate at random, but prevent all the defective homozygous recessive individuals from producing offspring. Each succeeding generation so produced we shall call F_1, F_2, and so on. Let n be the number of generations following the parent generation. Then any given generation is composed of the proportional number of individuals of each Mendelian class given by the formula:

$$F_n = (n+1)^2 AA + 2(n+1) Aa + 1\,aa.$$

This formula is derived from the formulas given by Jennings (1916: 68). In Table I are given the proportion of the three Mendelian classes after certain numbers of generations of adverse selection in a population made up according to the above stated assumptions. If selection is discontinued at any generation, the proportion of the several Mendelian classes then established will remain constant until there is further selection (Jennings, 1916: 64).

Adverse selection is shown by Table I to be very effective when the homozygous recessives form a considerable proportion of the population. When the recessives in a generation number 2778 per 100,000 of the whole population (F_4 of Table I), the effect of preventing their breeding would theoretically be to reduce the proportion of homozygous recessives in the following generation by more than 26 per cent.

As the number of homozygous recessives in a population becomes less, the effectiveness of adverse selection also becomes less. Nevertheless, in a population in which the homozygous recessives for any character number 100 per 100,000 of the individuals born, a decrease of over 6 per cent in the occurrence of the character should be produced by one generation of adverse selection. In a population in which there are 10 homozygous recessives in 100,000 of the population, a decrease of slightly over 2 per cent would theoretically be obtained by a single generation of adverse selection. Even in a population in which only one homozygous recessive individual occurs in 100,000 of the population, the decrease in the number of affected individuals secured by one generation of adverse selection should be approximately 0.63 per cent.

Although the effectiveness of adverse selection of this kind decreases with each decrease in the proportion of homozygous recessives, the rate of decrease in the effectiveness of adverse selection falls less rapidly than does the proportion of homozygotes in the population. In time, with continued adverse selection, the proportion of recessives in a population will be reduced to a negligible amount, although in a large population the recessive character theoretically can never completely be eliminated.

It may often happen that not all of the homozygous recessives in a generation can be prevented from breeding. If this happens, the effectiveness of the resulting adverse selection can be shown to be nearly but not exactly proportional to the number of recessives removed. The composition of the following generations may be calculated by the formula given by Jennings (1916: 65).

In a population, for example, composed of the Mendelian classes $1\,AA + 2\,Aa + 1\,aa$, if all the homozygous recessive *aa* individuals are prevented from breeding the reduction in the proportion of homozygous recessives in the following generation should be 55.56 per cent (Table I). If only half of the *aa* individuals are prevented from breeding, the reduction in their abundance in the following generation is 26.53 per cent. If only one-fourth or one-tenth of the *aa* individuals are prevented from breeding, the reduction in the next generation in the proportion of homozygous recessives is, respectively, 12.89 or 5.06 per cent. With a population containing a high proportion of homozygous recessives, the effectiveness of selection against the recessive, therefore, decreases slightly *more* rapidly than proportionally to the percentage of homozygotes prevented from breeding.

TABLE I

Effect of Adverse Selection Against a Recessive Character in a Population of Unlimited Size

All homozygous recessives removed before sexual maturity.
Random mating of the remaining population and equal fertility assumed.

Generation	Proportion in Each Mendelian Class			Homozygous Recessives per 100,000 Population	Percentage of Decrease in Homozygous Recessives from Next Previous Generation
	AA	*Aa*	*aa*		
P	1	2	1	25,000.00	....
F_{1}	4	4	1	11,111.11	55.56
F_{2}	9	6	1	6,250.00	43.75
F_{3}	16	8	1	4,000.00	36.00
F_{4}	25	10	1	2,777.78	30.56
F_{5}	36	12	1	2,040.81	26.53
F_{10}	121	22	1	694.44	15.97
F_{20}	441	42	1	206.61	8.88
F_{30}	961	62	1	97.66	6.15
F_{40}	1,681	82	1	56.69	4.71
F_{50}	2,601	102	1	36.98	3.81
F_{60}	3,721	122	1	26.01	3.20
F_{100}	10,201	202	1	9.61	1.95
F_{150}	22,801	302	1	4.33	1.31
F_{200}	40,401	402	1	2.45	.99
F_{250}	63,001	502	1	1.57	.79
F_{300}	90,601	602	1	1.10	.66
F_{400}	160,801	802	1	.62	.50
F_{500}	251,001	1,002	1	.40	.40
F_{600}	361,201	1,202	1	.28	.33
F_{700}	491,401	1,402	1	.20	.28
F_{800}	641,601	1,602	1	.16	.25
F_{1000}	1,002,001	2,002	1	.10	.20
F_{1200}	1,442,401	2,402	1	.07	.17
F_{1400}	1,962,801	2,802	1	.05	.14
F_{1600}	2,563,201	3,202	1	.04	.12
F_{1800}	3,243,601	3,602	1	.03	.11
F_{2000}	4,004,001	4,002	1	.02	.10

When the recessive gene is rare the results are somewhat different. In a hypothetical population with Mendelian classes in the proportion of 2500 $AA + 100\,Aa + 1\,aa$, if all the homozygous recessives are prevented from breeding, the reduction in homozygous recessives in the next generation will be 3.810 per cent. If, instead of all, only one-half, one-fourth, or one-tenth of the homozygous recessives are prevented from breeding, then the reduction in the number of homozygous recessives in the following generation will be, respectively, 1.914, 0.959, or 0.384 per cent. It follows that in a population in which the recessive gene is rare, as the percentage of homozygous recessives prevented from breeding becomes smaller the effectiveness of adverse selection decreases slightly *less* than proportionally.

The effectiveness of adverse selection, therefore, is closely proportional to the percentage of homozygous recessives allowed to breed. If, for example, one-tenth of the homozygous recessives are prevented from breeding, the resulting adverse selection is in the neighborhood of one-tenth as effective as if all the homozygous recessives were prevented from producing offspring. Weak adverse selection is slightly less than proportionally as effective as removal of all the homozygous recessives when the recessive gene is equal in abundance to the dominant gene, but it is slightly more than proportionally as effective when the recessive gene is rare in the population.

Should extremely rigorous selection against some recessive defect be desired, all the offspring from known heterozygous parents should be prevented from leaving descendants. The offspring of parents both of which are heterozygous for a given character are expected to be in the proportion of one entirely normal individual, two heterozygous but normal appearing individuals, and one homozygous recessive individual showing the defect. Therefore, if all the full brothers and sisters of each homozygous recessive are prevented from leaving offspring, the effectiveness of the resulting adverse selection in eliminating the defective heredity should on the average be twice what it would be if the homozygous recessives alone were denied parenthood.

The above calculations of the effectiveness of adverse selection against a recessive are based on the assumption of completely random mating in a population of unlimited size. In a small population in which the recessive gene is relatively rare the effectiveness of adverse selection may be much greater than that calculated. If the average number of heterozygotes per generation in a population approaches one the recessive character will be wholly lost should any generation by chance fail to include a heterozygous individual.

Not all hereditary defects, by any means, are recessive in heredity. Defects which are inherited as dominants, those inherited without dominance, and those which are sex-linked all respond to adverse selection much more readily than do recessive characters.

Characters which are inherited as dominants and which appear before sexual maturity can easily be eliminated from a population. All the individuals which carry a dominant hereditary factor show the character, no matter whether the factor be carried in the homozygous or in the heterozygous condition. Therefore, if all the individuals with a dominant defect are prevented from producing offspring, the character will be eliminated in one generation.

Characters which lack dominance in heredity are also not very difficult to eliminate. Most of the individuals carrying the undesired character in heterozygous condition will exhibit some trace of it, and, therefore, defective heredity of this type can also quickly be eliminated from a population.

Sex-linked recessive characters respond very readily to selection:

> Since the male has only one sex chromosome, all males who carry the recessive gene exhibit the recessive trait, unless special conditions of environment are essential to its manifestation. The eye defect called megalocornea and one type of hereditary optic atrophy (Leber's disease) belong to this class. Sterilization of all individuals displaying sex-linked recessive disease halves the proportion of persons affected in every generation.—Hogben (1933: 23).

Ordinary linkage between hereditary factors has only a negligible influence on the effectiveness of selection, because if more than a few generations are considered all the factors are distributed practically at random due to crossovers.

Some inherited defects are undoubtedly caused by multiple factors. If all the multiple factors producing a certain defect are completely recessive, the compound homozygous recessive will appear proportionally less frequently than will the homozygous recessive of any one of the factors concerned. When the compound homozygous recessive is prevented from breeding, therefore, only a proportional fraction of the homozygous recessives for any one factor is removed from the population. If, for example, ten factors are involved, only one-tenth of the homozygous recessives of each factor is eliminated when the compound homozygous recessive is prevented from breeding. Earlier in this paper it has been pointed out that the effectiveness of partial adverse selection is approximately proportional to the percentage of homozygous recessives prevented from breeding. Then, if one-tenth of the homozygous recessives of each of ten multiple recessive factors is removed, the effect is about the same as if all the homozygous recessives of one factor are prevented from leaving offspring. In other words, adverse selection will be approximately as effective against a defect produced by multiple recessive factors as against a defect produced by a single recessive factor. Adverse selection against defects produced by multiple factors which are rare in the population, moreover, should theoretically be slightly more efficient than adverse selection would be against a defect produced by a single recessive factor.

Not all multiple factors are necessarily recessive. Selection against a character produced by multiple factors some of which either are dominant, are without dominance, or are sex-linked, would of course be more effective than selection against multiple factors all of which are recessive.

SUMMARY

Adverse selection against a defective recessive character is most effective when the homozygous recessive individuals constitute a considerable proportion of the population. As the number of homozygous recessives in the population decreases the expected rate of elimination of the defectives by adverse selection also decreases, but this decrease in rate is much less rapid than the decrease in the proportion of defectives. A reduction of slightly over 2 per cent per generation in the number of defectives will theoretically be secured by preventing the reproduction of all homozygous recessives when there are only ten defectives, all due to the same hereditary factor, in 100,000 population. The expected reduction in defectives is approximately 0.63 per cent per generation even when the number of homozygous recessives has been reduced to one per 100,000 population. Defective characters which are inherited through dominant factors, through factors lacking dominance, or through sex-linked factors, respond much more readily to adverse selection than do recessive characters.

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